File No. 16051-7US CC/DBB/iw

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Andrew VAILLANT et al.
Serial Number:	10/661,402
Filing Date:	September 12, 2003
For:	ANTIVIRAL OLIGONUCLEOTIDES TARGETING VIRAL FAMILIES
Art Unit:	1648
Examiner:	HURT, Sharon L.
Agent:	Cawthorn, Christian Direct Line: (514) 847-4256

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
U. S. A.

Sir:

Enclosed herewith is Form PTO/SB/33, i.e. a Pre-Appeal Brief Request for Review. Please consider the reasons set out below for which the review is being requested.

A Notice of Appeal is being filed concurrently.

REASONS:

Claims 52-56 have been rejected under 35 U.S.C. 102(e) as being anticipated by Peyman *et al.* The Examiner stated that in the previous response, the argument submitted with respect to the fact that Peyman *et al.* only teaches that the efficacy of the tested oligonucleotides is dependent on the presence of 10 guanines extension at each extremity of the oligonucleotide was not convincing. The Examiner alleges that this argument relates to the G-quartet structures which are not mentioned in the claims. Furthermore, the Examiner alleges that Peyman *et al.* teaches administering the same oligonucleotides as those of the claimed invention (oligonucleotides of at least 10 nucleotides in length) and teaches administering the oligonucleotides to the same patient population as the present invention. Therefore, since Peyman teaches administering the same composition to the same patient population, the method of Peyman anticipates the claimed invention. It is worth mentioning

that the Examiner concluded that the oligonucleotide composition of Peyman has antiviral activity acting by a non-sequence complementary mode of action, even though nowhere in Peyman is it disclosed that the taught oligonucleotides have such antiviral activity acting by a non-sequence complementary mode of action. It is believed that the Examiner has concluded in this manner in hindsight.

In this regard, Applicants submit that nowhere is it taught or even suggested in Peyman *et al.* that oligonucleotides have antiviral activity against multiple viruses acting by a non-sequence complementary mode of action. Drawing that teaching or suggestion from Peyman *et al.* is only the result of hindsight from Applicants' own application. Moreover, Peyman *et al.* only enabled four antisense oligonucleotides against HSV-1 in cell culture (as disclosed in column 14, lines 14-19 in Peyman). Peyman *et al.* only teaches how to stabilize and improve cell penetration by capping antisense oligonucleotides (with the addition of a cap of guanine at their extremities). In column 6, lines 8-9, Peyman *et al.* teaches that the effective oligonucleotides are understood to mean antisense oligonucleotides. By definition, an "antisense" is a molecule that interacts with complementary strands of nucleic acids, modifying the expression of genes. Consequently, a person skilled in the art would recognize that an antisense RNA or single-stranded antisense DNA is a molecule which is complementary to the nucleic acid sequence of a gene of interest. Thus, the mechanism of action of an antisense is dependent on the specific sequence, since it must be complementary to a strand of a nucleic acid in order to interact and modify the expression of the gene of interest. In addition, a person skilled in the art will readily recognize, upon searching in databases, that SEQ ID NOs: 1-34 disclosed by Peyman *et al.* only represent sequences that are complementary to known genes, and thus represent antisense oligonucleotides. Applicants previously submitted a Table identifying the gene targeted by these antisenses (see the last response filed April 11, 2007). In column 6, lines 30-31; column 8, lines 29-30; column 10, lines 35-36; column 11, lines 4-5; and column 14, lines 14-19 of Peyman *et al.*, it is clearly stated that the oligonucleotides represented by SEQ ID NOs: 35-105 are examples of novel antisense effective against specific targets. All sequences listed in Peyman's patent are complementary to target sequences.

Assistant Commissioner for Patents

Consequently, SEQ ID NOs: 1-105 all represent antisense oligonucleotides which are complementary to a portion of the nucleic acid sequence of a specific gene. Thus, by its inherent properties, as well as by definition, an antisense will modify the expression of a gene by a sequence complementary mode of action. This is reflected in independent claim 1 of Peyman *et al.* where an oligonucleotide having a nucleotide sequence complementary to a target sequence flanked by a Cap of guanines is claimed. To the contrary, Applicants submit that the present application claims a method for selecting an antiviral oligonucleotide, wherein the anti-viral activity of said oligonucleotides occurs principally by a non-sequence complementary mode of action, as submitted hereinabove, and which is suggested nowhere in Peyman *et al.*

In addition, Peyman *et al.* discloses (in columns 1 and 2, under Summary), oligonucleotides having antiviral activity because they are antisenses and which have a Cap of guanine(s) at its 5' and/or 3' extremity to stabilize and improve cell penetration. To the contrary, the oligonucleotides disclosed in the present invention do not have to be antisenses, nor do they need to have a Cap of guanines in order to have antiviral activity. Once again, a person skilled in the art would recognize that Peyman *et al.* teach antisense oligonucleotides wherein stabilization depends on the presence of a Cap of guanines and the antiviral activity depends on the sequence of the antisense oligonucleotide. Thus, the stabilization of the antisenses disclosed in Peyman is dependent on the presence of a secondary structure since, as stated in Peyman *et al.* (see column 1, lines 55-57), oligonucleotides which contain short segments of G residues are able to form intramolecular structures called G-quartets. Thus, not only is the antiviral activity dependent on the sequence, but the stabilization of the antisenses disclosed in Peyman is sequence dependent (in order to form the G-quartet structure).

In view of the arguments presented hereinabove, it is believed that the claims now on file are novel in view of Peyman *et al.*, and thus Applicants respectfully submit that the 35 U.S.C. §102(e) rejection over Peyman *et al.* is improper, and request that it be withdrawn.

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Double Patenting

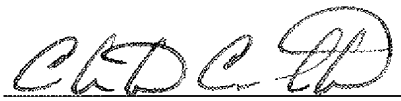
The Examiner has maintained her rejection of claims 52-56 on the grounds of non-statutory double-patenting over claims 53-57 of co-pending Application No. 10/969,812. Applicants submit that this rejection should now be moot in light of the Terminal Disclaimer under 37 C.F.R. §1.321 which was filed June 14, 2007.

In view of the foregoing, Applicants respectfully request that the double-patenting rejections be withdrawn.

It is submitted, therefore, that the claims are in condition for allowance, and prompt and favorable action in the form of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

Date: June 14, 2007

By: 

Christian Cawthorn, Reg. No. 47,352
Agent for Applicants
Tel: (514) 847-4256

OGILVY RENAULT LLP
1981 McGill College, Suite 1600
Montreal, Quebec H3A 2Y3
CANADA

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